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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/083,793	05/22/1998	BRIAN R. MURPHY	17634-000320	4558

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NATIONAL INSTITUTES OF HEALTH
OFFICE OF TECHNOLOGY TRANSFER
6011 EXECUTIVE BLVD SUITE 325
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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/083,793	MURPHY ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *144-155,157-190 and 192-215* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *144-155,157-190 and 192-215* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 May 1998* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed on March 15, 2006 is acknowledged and entered. Claims 144-155, 157-190 and 192-215 are pending and under examination.

Claim Rejections - 35 USC § 112

2. (*New Rejection*) Claims 146-155, 157-190 and 192-215 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 146 recites, "said polynucleotide comprising the complement of nucleotide sequences of SEQ ID NOS: 69, 71 and 73". The metes and bounds of the phrase cannot be determined. Does the polynucleotide comprise the complement sequences of all of SEQ ID NOS: 69, 71 and 73? The term, "complement of nucleotide sequence of SEQ ID NOS: 69, 71 and 73" implies either a grammatical error, or that Applicant intends to claims complement sequence of fragments of SEQ ID NOS: 69, 71 and 73. Clarification is required.

Claims 214 and 215 are rejected because they depend from cancelled claims. Correction is required.

Claim Rejections - 35 USC § 102

3. The rejection of claims 144-165, 182-200, 207 and 208 under 35 U.S.C. 102(e) as being anticipated by Belshe *et al.* (US 5,869,036, "Belshe"), is moot with respect to cancelled claims, and withdrawn with regard to pending claims in view of Applicant's persuasive arguments.

Applicant argues that SEQ ID NO: 61, 63, 65, 67, 69, 71 and 73 differ from the cp45 genome described in Belshe. Applicant points out that SEQ ID NOS: 63 and 73 include two mutations in a codon in the F protein-encoding region and L protein-coding region, respectively. The corresponding codons in the cp45 genome contain a single mutation. Applicant also points out that SEQ ID NOS: 61, 63, 65 and 67 include restriction sites *Hpa I, Sca I, Bam HI* and *BstXI*, respectively. These restriction sites are not present at the corresponding locations of the cp45 genome. Applicant finally points out that SEQ ID NOS: 69, 71 and 73 does not include the *EaeI, Bsr I* and *Ava II* restriction sites. These sites are present in the cp45 genome corresponding locations. Applicant concludes that Belshe does not anticipate the claims. In response to Applicant's arguments, the Office agrees that Belshe's cp45 genome does not contain any of the claimed sequences (SEQ ID NO: 61, 63, 65, 67, 69, 71 and 73).

With regard to the claims that recite, "said partial or complete PIV genome or antigenome comprising a polynucleotide encoding a wild-type L protein of the PIV", the limitation distinguishes the claims from Belshe. Applicant argues, and the examiner agrees that Example 5 is directed to a complementation assay, wherein the L gene (among others) was introduced into a plasmid. CV-1 cells were co-transfected with the plasmid vector pRSV-T and one or more recombinant plasmids, such as the L gene. Twenty-four hours post-transfection, the expressing cells were infected with cp45 virus. Based on this complementation assay, Belshe concludes that cp45 viruses complemented with the wild-type L protein, produced by the cell, are capable of replicating at the non-permissive temperature for the cp45 virus (col. 16, lines 54-62). The wild-type L gene is not incorporated into the genome (as required by the claims). Therefore, Belshe does not teach or suggest the invention as claimed.

Claim Rejections - 35 USC § 103

4. The rejection of claims 172-173, 179-190, 192-200, 207 and 208 under 35 U.S.C. 103(a) as being unpatentable over Belshe, is withdrawn in view of Applicant's persuasive arguments and amendments. With reference to claims 172-173, 179-190, 192-200, 207 and 208, the claims either recite sequences containing mutations/restriction sites that are present/absent from the cp45 genome of Belshe, or, the claims require that a wild-type L gene be present in the genome of the virus particle. These limitations distinguish the instant claims from Belshe, for reasons described above.

5. The rejection of claims 166-171, 174-178, 201-206, 209-215 under 35 U.S.C. 103(a) as being unpatentable over Belshe is maintained for reasons of record. The claims encompass embodiments wherein the genome comprises additional mutations found in the *cp*45 genome. The teachings of Belshe are summarized above. Belshe teaches the mutations of the *cp*45 genome (col. 5-6) and uses the genome as a template to insert foreign sequences (col. 9-10). The act of recombining the cp45 genome with heterologous sequences reads on the instant claims. The resulting virus contains the cp45 mutations in addition to the heterologous sequences.

Also claimed is a virus wherein the heterologous antigenic determinant comprises a transcription unit (that encodes an open reading frame) is inserted between a gene start and a gene end sequence of the PIV background genome. This limitation does not lend patentability to the claimed invention because insertion of heterologous gene encoding the antigenic determinant would only be appropriate between a gene start and gene end sequence. One would have been

motivated to use the gene start and gene end sequences of Belshe's background PIV in order to retain as much stability as possible when expressing the heterologous genes. One would have had a reasonable expectation of success given the fundamental nature of recombination and the desire to obtain stable expression. Therefore, the claimed subject matter would have been obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments have been carefully considered but fail to persuade. Applicant argues that Belshe only discloses that the "gene sequence which encodes [the desired protein]...may be substituted for the corresponding sequence in the cp45 genome", (Belshe, col. 8, lines 59-61). Applicant points to Belshe's Figure 1, which does not depict any non-translated, intergenic sequences. Applicant argues that the Office's analysis of obviousness relies on improper hindsight.

In response to Applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In this case, one would have been motivated to use the gene start and gene end sequences of Belshe's background PIV in order to retain as much stability as possible when expressing the heterologous genes. Belshe teaches that "the region of the genome of the target virus that encodes one or more surface glycoproteins may be combined with the regions of the cp45

genome related to replication and internal structure of the virus", see col. 8, lines 59-66. As for Figure 1, it is a schematic representation of the HPIV-3 viral genome with the attenuation mutations (cp45). Figure 1 does not appear to indicate anything about inserting heterologous sequences, and thus is not relevant to insertion of heterologous genes. One would have had a reasonable expectation of success given the fundamental nature of recombination and the desire to obtain stable expression. Securing stable expression is not a concept from Belshe, rather, from the knowledge of one or ordinary skill in the art generally relating to recombination and heterologous gene expression. Therefore, the rejection is maintained for reasons of record.

Double Patenting

6. Claims 144-155, 157-190 and 192-215 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53-85 of copending Application No. 09/458,813. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is a species of the instantly claimed genus of PIVs, rendering the genus claims obvious. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 144-155, 157-190 and 192-215 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 and 46-74 of copending Application No. 09/459,062. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending

application is a species of the instantly claimed genus of PIVs, rendering the genus claims obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 144-155, 157-190 and 192-215 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 85, 88-92, 94-96, 98, 99, 101, 104, 107, 108, 113-117, 119, 122-126, 128-130, 132, 133, 135, 140, 141, 146-152, 154, 157, 159, 162 and 163 of copending Application No. 09/586,479. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is a species of the instantly claimed genus of PIVs, rendering the genus claims obvious. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 144-155, 157-190 and 192-215 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 180-222 of copending Application No. 09/733,692. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is a species of the instantly claimed genus of PIVs, rendering the genus claims obvious. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

10. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen 4/18/2006

Stacy B. Chen
Primary Examiner
April 18, 2006